

Fig. 1

ATGTCCATGA	ACTGCTGAGT	GGATAAACAG	CACGGGATAT	CTCTGTCTAA	- 96
AGGAATATTA	CTACACCAGG	AAAAGGACAC	ATTCGACAAC	AGGAAAGGAG	- 46
CCTGTCACAG	AAAACCACAG	TGTCCTGTGC	ATGTGACATT	TCGCC	- 1
ATG GGA AAC AAC TGT TAC AAC GTG GTG GTC ATT GTG CTG CTG CTA	45				
Mbt Gly Asn Asn Cys Tyr Asn Val Val Val Ile Val Leu Leu Leu					
GTG GGC TGT GAG AAG GTG GGA GCC GTG CAG AAC TCC TGT GAT AAC	90				
Val Gly Cys Glu Lys Val Gly Ala Val Gln Asn Ser Cys Asp Asn					
TGT CAG CCT GGT ACT TTC TGC AGA AAA TAC AAT CCA GTC TGC AAG	135				
Cys Gln Pro Gly Thr Phe Cys Arg Lys Tyr Asn Pro Val Cys Lys					
● H4-1BB FI ●					
AGC TGC CCT CCA AGT ACC TTC TCC AGC ATA GGT GGA CAG CCG AAC	180				
Ser Cys Pro Pro Ser Thr Phe Ser Ser Ile Gly Gly Gln Pro Asn					
● H4-1BB FII					
TGT AAC ATC TGC AGA GTG TGT GCA GGC TAT TTC AGG TTC AAG AAG	225				
Cys Asn Ile Cys Arg Val Cys Ala Gly Tyr Phe Arg Phe Lys Lys					
TTT TGC TCC TCT ACC CAC AAC GCG GAG TGT GAG TGC ATT GAA GGA	270				
Phe Cys Ser Ser Thr His Asn Ala Glu Cys Glu Cys Ile Glu Gly					
TTC CAT TGC TTG GGG CCA CAG TGC ACC AGA TGT GAA AAG GAC TGC	315				
Phe His Cys Leu Gly Pro Gln Cys Thr Arg Cys Glu Lys Asp Cys					
AGG CCT GGC CAG GAG CTA ACG AAG CAG GGT TGC AAA ACC TGT AGC	360				
Arg Pro Gly Gln Glu Leu Thr Lys Gln Gly Cys Lys Thr Cys Ser					
● H4-1BB RI ●					
TTG GGA ACA TTT AAT GAC CAG AAC GGT ACT GGC GTC TGT CGA CCC	405				
Leu Gly Thr Phe Asn Asp Gln Asn Gly Thr Gly Val Cys Arg Pro					
← H4-1BB RII					
TGG ACG AAC TGC TCT CTA GAC GGA AGG TCT GTG CTT AAG ACC GGG	450				
Trp Thr Asn Cys Ser Leu Asp Gly Arg Ser Val Leu Lys Thr Gly					
ACC ACG GAG AAG GAC GTG GTG TGT GGA CCC CCT GTG GTG AGC TTC	495				
Thr Thr Glu Lys Asp Val Val Cys Gly Pro Pro Val Val Ser Phe					
TCT CCC AGT ACC ACC ATT TCT GTG ACT CCA GAG GGA GGA CCA GGA	540				
Ser Pro Ser Thr Thr Ile Ser Val Thr Pro Glu Gly Gly Pro Gly					
GGG CAC TCC TTG CAG GTC CTT ACC TTG TTC CTG GCG CTG ACA TCG	585				
Gly His Ser Leu Gln Val Leu Thr Leu Phe Leu Ala Leu Thr Ser					
GCT TTG CTG CTG GCC CTG ATC TTC ATT ACT CTC CTG TTC TCT GTG	630				
Ala Leu Leu Leu Ala Leu Ile Phe Ile Thr Leu Leu Phe Ser Val					
CTC AAA TGG ATC AGG AAA AAA TTC CCC CAC ATA TTC AAG CAA CCA	675				
Leu Lys Trp Ile Arg Lys Lys Phe Pro His Ile Phe Lys Gln Pro					
TTT AAG AAG ACC ACT GGA GCA GCT CAA GAG GAA GAT GCT TGT AGC	720				
Phe Lys Lys Thr Thr Gly Ala Ala Gln Glu Glu Asp Ala Cys Ser					

Fig.1 cont'd

TGC CGA TGT CCA CAG GAA GAA GAA GGA GGA GGA GGA GGC TAT GAG 785
 Cys Arg Cys Pro Glu Glu Glu Gly Gly Gly Gly Gly Tyr Glu

CTG TGA 771
 Leu ---

TGTA	CTATCC	TAGG	AGATGT	GTGG	GCCGAA	ACCG	GAGAAGC	ACTAG	GACCC	821
CACCA	TCCTG	TGGA	ACAGCA	CAAG	CAACCC	CACC	ACCCTG	TTCT	TACACA	871
TCAT	CCTAGA	TGAT	GTGTGG	GCGC	GCACCT	CATC	CAAGTC	TCTT	CTAACG	921
CTAA	CATATT	TGTC	TTTACC	TTTT	TTTAAAT	CTTT	TTTTTAA	ATTT	AAATTT	971
TATGT	GTGTG	AGTG	TTTTGC	CTGC	CTGTAT	GCAC	ACGTGT	GTGT	GTGTGT	1021
GTGT	GTGACA	CTCT	GATGC	CTGA	GAGAGT	CAGA	AAGACAA	AGGG	TGGTT	1071
CCATA	AAGAAC	TGGAG	TTATG	GATGG	CTGTG	AGCC	GGNNNG	ATAG	GTCGGG	1121
ACGG	GACCT	GTCT	TCTTAT	TTTA	ACGTGA	CTGT	ATAATA	AAAA	AAAAAT	1171
GATATT	TCGG	GAATT	GTAGA	GATT	GTCTG	ACAC	CCTTCT	AGTT	AATGAT	1221
CTAAG	AGGAA	TTGTT	GATAC	GTAG	TATACT	GTAT	ATGTGT	ATGT	TATATGT	1271
ATATG	TATAT	ATAAG	ACTCT	TTTA	CTGTCA	AAGT	CAACCT	AGAG	TGTCTG	1321
GTTAC	CAGGT	CAATTT	TATT	GGAC	ATTTTA	CGTC	CACACAC	ACAC	CACACAC	1371
ACAC	CACAC	ACGTT	TATAC	TACG	TACTGT	TATC	GGTATT	CTAC	GTCATA	1421
TAAT	GGGATA	GGGT	AAAAAG	AAAC	CAAGA	GTGA	GTGATA	TTAT	TGTGGA	1471
GGTG	ACAGAC	TACCC	CTTCT	GGGT	ACGTAG	GGAC	AGACCT	CCTT	CGGACT	1521
GTCT	AAAACT	CCCC	TTAGAA	GTCT	CGTCAA	GTT	CCCCGAC	GAAG	AGGACA	1571
GAGG	AGACAC	AGTCC	GAAAA	GTTA	TTTTTC	CGG	CAATCC	TTTC	CCCTGTT	1621
TCGT	GACACT	CCAC	CCCTTG	TGG	ACACTTG	AGTG	TCATCC	TTGC	GCCGGA	1671
AGGT	CAGGTG	GTACC	CGTCT	GTAG	GGGCGG	GGAG	ACAGAG	CCGC	GGGGGA	1721
GCTAC	GAGAA	TCGAC	TACA	GGGC	GCCCCG	GGCT	TCGCAA	ATGA	AACTTT	1771
TTTA	ATCTCA	CAAG	TTTCGT	CCGG	GCTCGG	CGGA	CCTATG	GCGT	CGATCC	1821
TTATT	ACCTT	ATCCT	GCGCG	CAAG	ATAAAA	CAAC	CAAAAG	CCTT	GACTCC	1871
GGTA	CTAATT	CTCC	TGCCG	GCCCC	CGTAA	GCAT	AACGCG	GCGA	TCTCCA	1921
CTTT	AAGAAC	CTGG	CCGCGT	TCTG	CCCTGGT	CTCG	CTTTTCG	TAA	ACGGTTC	1971
TTACA	AAAAGT	AATT	AGTTCT	TGCT	TTTCAGC	CTCC	AAGCTT	CTG	CTAGTCT	2021
ATGG	CAGCAT	CAAG	GCTGGT	ATTT	GCTACG	GCTG	ACCGCT	ACGC	CGCCGC	2071
AATA	AAGGGTA	CTGG	GCGGCC	CGTC	GAAAGGC	CCTT	TGGTTT	CAGA	AAACCCA	2121
AGGC	CCCCCT	CATA	CCAACG	TTTC	GACTTT	GATT	CTTGCC	GGTA	CGTGGT	2171
GGTGG	GTGCC	TTAG	CTCTTT	CTCG	ATAGTT	AGAC				2205

Fig. 2a

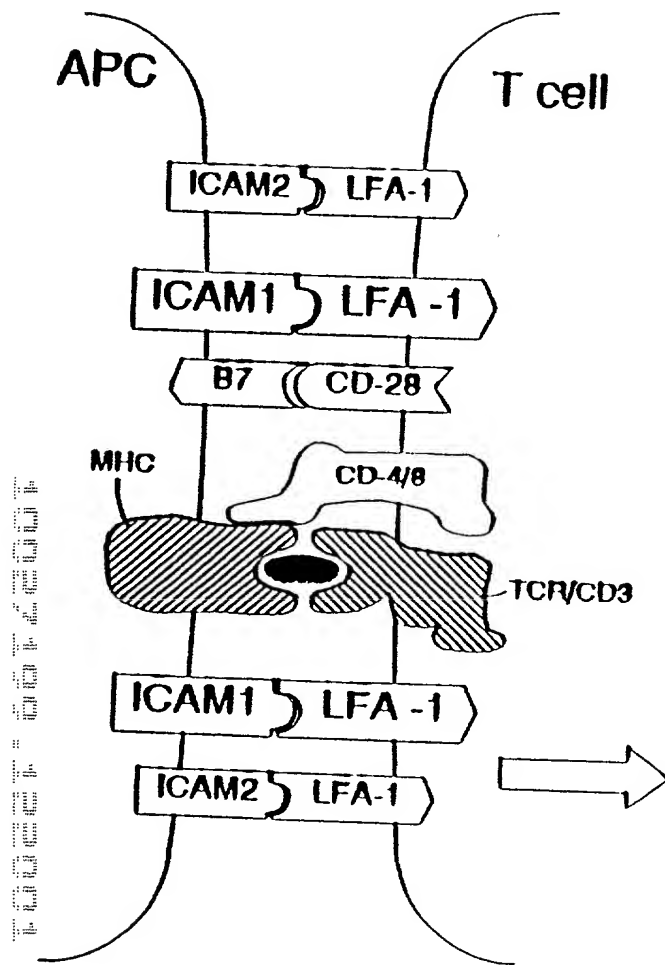
human homologue of mouse 4-1bb

h4-1bb Length 838

1 AATCAGCTTT GCTAGTATCA TACCTGTGCC AGATTTTCATC ATGGGAAACA
 51 GCTGTTACAA CATAGTAGCC ACTCTGTTGC TGGTCCTCAA CTTTGAGAGG
 101 ACAAGATCAT TGCAGGATCC TTGTAGTAAC TGCCCAGCTG GTACATTCTG
 151 TGATAATAAC AGGAATCAGA TTTGCAGTCC CTGTCCTCCA AATAGTTTCT
 201 CCAGCGCAGG TGGACAAAGG ACCTGTGACA TATGCAGGCA GTGTAAAGGT
 251 GTTTTTCAGGA CCAGGAAGGA GTGTTCTCTC ACCAGCAATG CAGAGTGTGA
 301 CTGCACTCCA GGGTTTCACT GCCTGGGGGC AGGATGCAGC ATGTGTGAAC
 351 AGGATTGTAA ACAAGGTCAA GAAC TGACAA AAAAAGGTTG TAAAGACTGT
 401 TGCTTTGGGA CATTTAACGA TCAGAAACGT GGCATCTGTC GACCCTGGAC
 451 AAAC TGTCTT TTGGATGGAA AGTCTGTGCT TGTGAATGGG ACGAAGGAGA
 501 GGGACGTGGT CTGTGGACCA TCTCCAGCTG ACCTCTCTCC GGGAGCATCC
 551 TCTGTGACCC CGCCTGCCCC TGCGAGAGAG CCAGGACACT CTCCGCAGAT
 601 CATCTCCTTC TTTCTTGCGC TGACGTGAC TGCCTTGCTC TTCCTGCTGT
 651 TCTTCCTCAC GCTCCGTTTC TCTGTTGTTA AACGGGGCAG AAAGAAACTC
 701 CTGTATATAT TCAAACAACC ATTTATGAGA CCAGTACAAA CTA CTCAAGA
 751 GGAAGATGGC TGTAGCTGCC GATTTCCAGA AGAAGAAGAA GGAGGATGTG
 801 AACTGTGAAA TGGAAGTCAA TAGGGCTGTT GGGACTTT

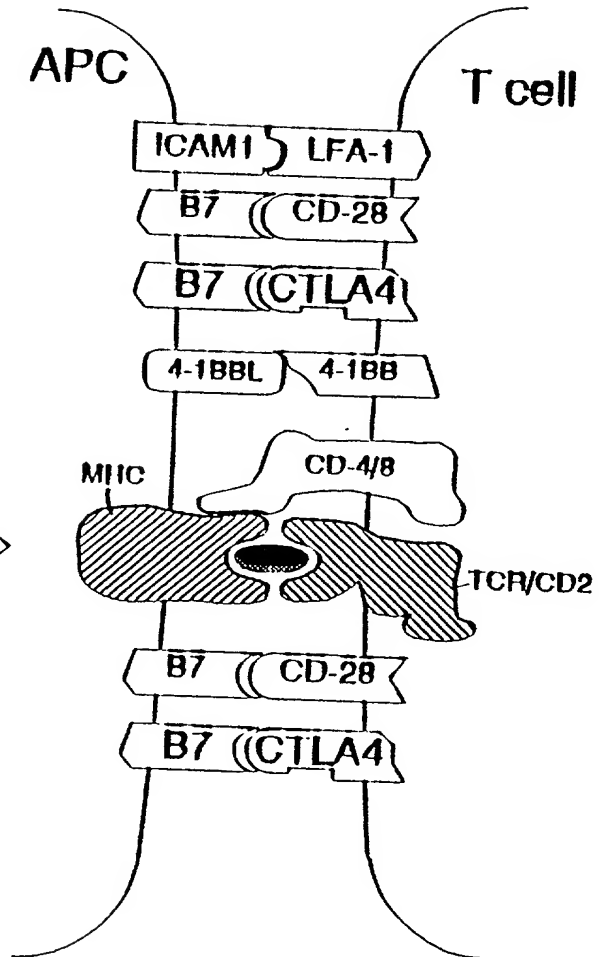
Fig. 2b

1 MGNSCYNIVA TLLLVLNFER TRSLQDFCSN CPAGTFCDNN RNQICSPCPP
 51 NSFSSAGGQR TCDICRQCKG VFRTRKECSS TSNAECDCTP GFHCLGAGCS
 101 MCEQDCKQGG ELTKKGCKDC CFGTFNDQKR GICRPWTNCS LDGKSVLVNG
 151 TKERDVVCGP SPADLSPGAS SVTPPAPARE FGHSPQIISF FLALTSTALL
 201 FLLFFLTLRF SVVKRGRKKL LYIFKQPFMR PVQTTQEEDG CSCRFPEEEE
 251 GGCEL



COGNITIVE PHASE
early activation

Fig. 3a



PROLIFERATION
CLONAL EXPANSION
late activation

Fig. 3b

NORMAL T-CELL ACTIVATION PATHWAY

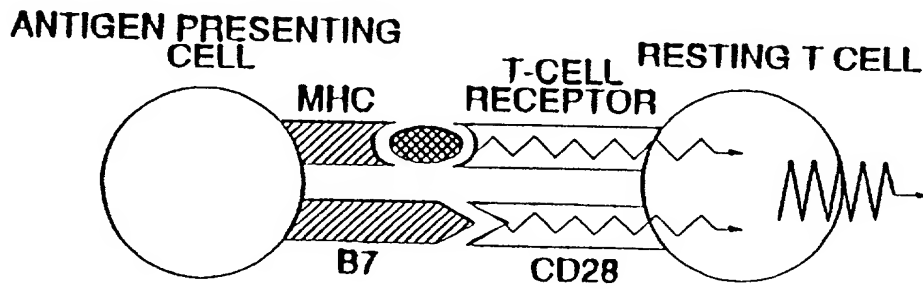


Fig. 4a

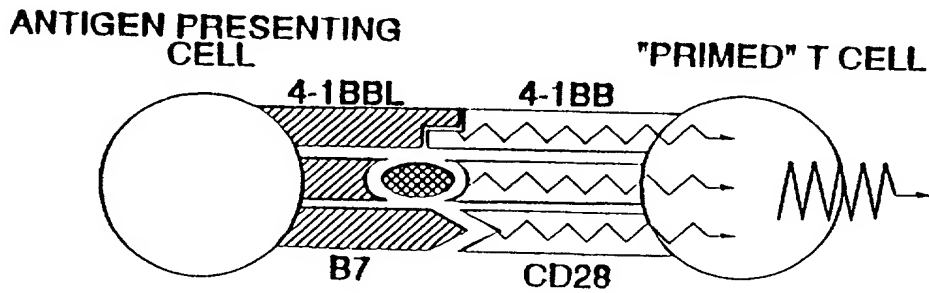


Fig. 4b

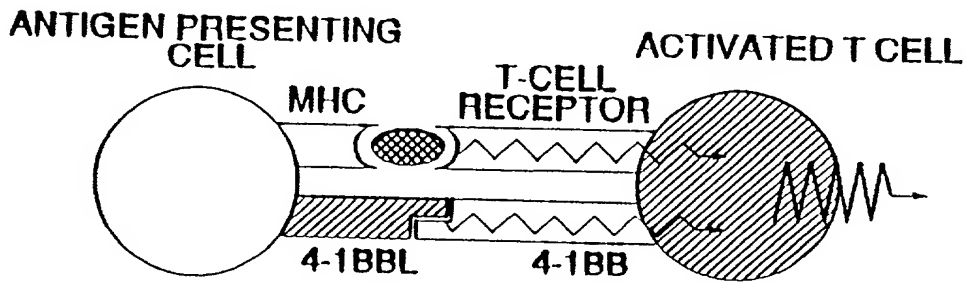


Fig. 4c

FIG. 4a, 4b, 4c

BLOCKING STEPS IN T-CELL ACTIVATION PATHWAY

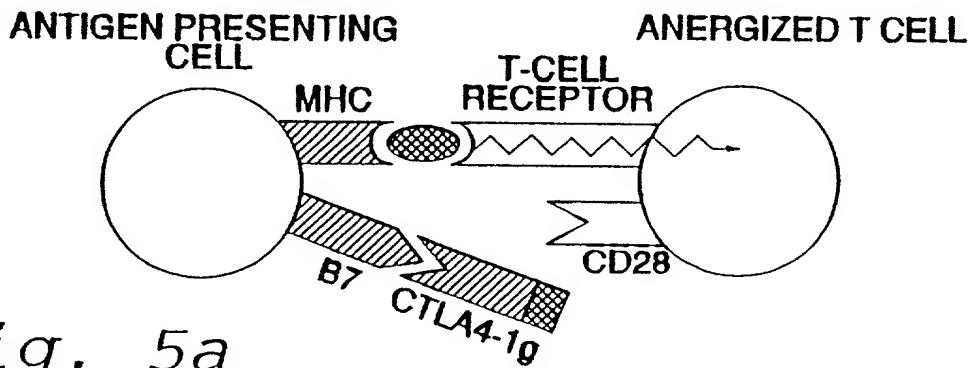


Fig. 5a

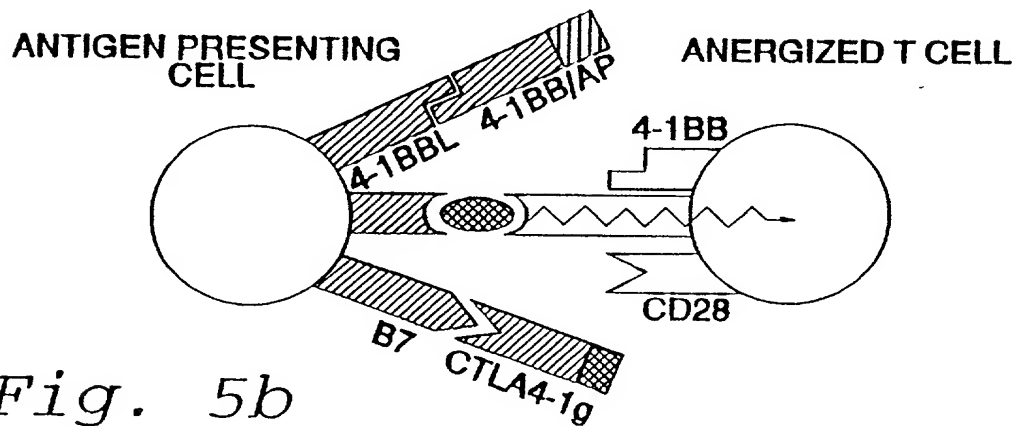


Fig. 5b

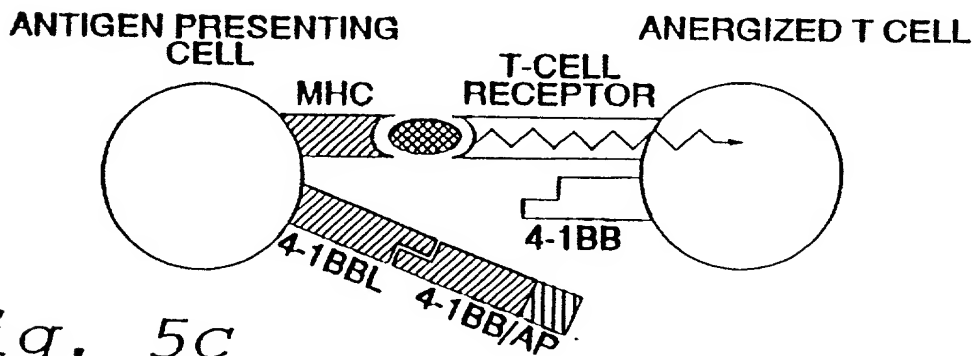


Fig. 5c